REMARKS

CLAIM STATUS

Claims 193-238 are pending in this application. Claims 193-207, 212, 219-227, and 232 have been amended. Claims 208-211, 213-218, 228-231, and 233-238 have been canceled without prejudice to Applicant's right to prosecute those subject matters in a future application.

REJECTION UNDER 35 USC § 103(a)

1. Claims 193-198, 208-224, and 228-238 are rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939). The rejection is respectfully traversed.

The present invention is drawn to a composition comprising a complement-activating antibody and an orally administered barley glucan that can enhance the anti-tumor effect of the antibody. Recently, the Supreme Court addressed the issue of obviousness and confirmed the test for obviousness as:

> Under §103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. at 1734 (quoting *Graham v. John Deere Co. of Kansas City*, 383 U.S. at 17-18).

In view of the above standard, Applicant submits that the Examiner has not undertaken a detailed analysis to determine the scope and content of the prior art, to ascertain the differences between the

prior art and the claims at issue, and to consider secondary considerations such as long felt but unsolved needs.

Yan et al. teach treatment combining glucan-rich soluble polysaccharides administered intravenously with an anti-tumor antibody resulted in enhanced anti-tumor response (see e.g. Figure 3). The Examiner acknowledges that Yan et al. do not teach or suggest using orally administered beta-glucan. Jamas et al. disclose (without providing any data) that a soluble glucan composition prepared according to the method disclosed therein could be administered orally to produce immune system enhancement (column 4, lines 40-45). Jamas et al., however, only present data on intravenous administration of glucan composition (see Examples 5-6) that caused an increase in white blood cell counts in mice (Example 5) or protection in a murine sepsis model (Example 6). Jamas et al. do not teach or suggest orally administered barley glucan can be used to enhance anti-tumor effect of a complement-activating antibody as claimed herein.

Hence, the scope and content of Yan et al. and Jamas et al. only teach intravenously administered glucan can enhance anti-tumor response of an anti-tumor antibody. Yan et al. and Jamas et al., however, do not provide any support or data on whether orally administered barley glucan can be used to enhance anti-tumor effect of a complement-activating antibody.

The Examiner contends that the prior art does disclose orally administered beta glucan has a systemic immunostimulating effect, and cites the references of Harada et al. (1997) and Nanba et al. (1987, 1997) as support (page 7, Final Office Action mailed August 7, 2007). Applicant submits, however, the references cited by the Examiner do not teach or suggest orally administered barley glucan can be used to

enhance anti-tumor effect of a complement-activating antibody as claimed herein. Harada et al. (1997) only teach orally administered PSK, a protein-bound polysaccharide derived from Basidiomycetes, can enhance anti-tumor CD4+ T cell response. Nanba et al. (1987) and Nanba and Kuroda (1987) disclose the powdered fruit bodies of shiitake showed anti-tumor activity when given orally to mice. Nanba and Kubo (1997) only teach protein-bound beta-glucan (D-fraction) extracted from Maitake mushroom has the ability to inhibit tumor growth, increase H2O2 production from macrophages and increase cytotoxic T cell activity. Taken together, the above cited references disclose stimulatory effects of glucan on various immune cell types such as CD4+ T cells and cytotoxic T cells. The scope and content of the above cited references, however, do not teach or suggest orally administered barley glucan would enhance anti-tumor effect of a complement-activating antibody as claimed herein.

The Examiner contends that any reference whatsoever in the prior art that indicates a therapeutic agent can be administered orally to produce a systemic effect is sufficient teaching to provide a reasonable expectation of success in administering that agent orally (page 7, final office action mailed August 7, 2007). Applicant submits, however, the present invention is not drawn to orally administering an agent to produce a systemic effect. The present invention instead is drawn to a composition comprising orally administered barley glucan that can enhance the anti-tumor effect of a complement-activating antibody.

Applicant further submits that the cited prior art do not provide a reasonable expectation of success in practicing the invention claimed herein because the glucans disclosed in the prior art cannot enhance anti-tumor effect of a complement-activating antibody as disclosed herein. Figure 7 shows that PSK (the glucan disclosed in Harada et

al. (1997)) cannot enhance anti-tumor effect of a complement-activating antibody (see page 8, line 30 to page 9, line 2). Similarly, Figure 8 shows that the D-fraction extracted from Maitake mushroom (the glucan disclosed in Nanba and Kubo (1997)) cannot enhance anti-tumor effect of a complement-activating antibody (see page 9, lines 4-8). In contrast, the present specification shows that beta-glucan from barley displays synergistic anti-tumor effect with a complement-activating antibody (see Figures 7-8).

In addition to the unexpected results or lack of reasonable expectation of success discussed above, Applicant further submits that the present invention fulfills a long felt but unsolved needs. One of ordinary skill in the art would readily recognize oral administration is a more convenient, less painful and less expensive method of delivering a therapeutic agent. Yet the literature on beta-glucan, in its entirety, does not report even a single instance of combining orally administered glucan with any kind of antibody until Applicant's work was published. In view of the well-recognized advantages of oral administration, the lack of report in the prior art on using orally administered glucan to enhance anti-tumor effect of a complement-activating antibody indicates that one of ordinary skill in the art generally believe that oral administration of beta-glucan is not workable. In other words, enhancing the anti-tumor effect of a complement-activating antibody by an orally administered agent is a long felt but unsolved needs, and the present invention fulfills such needs.

Taking the totality of the case into consideration, Applicant submits that the difference between the prior art and the claims at issue is that the prior art does not teach or suggest orally administered barley glucan can be used to enhance anti-tumor effect of a complement-activating antibody. The prior art also does not provide

a reasonable expectation of success in practicing the claimed method, especially in view of the fact that glucans described in the prior art are not effective in the method claimed herein. Moreover, the present invention fulfills a long felt but unsolved needs.

In view of the above remarks, Applicant submits that combination of Yan et al. and Jamas et al. does not render claims 193 and 219 obvious. Claims 208-211, 213-218, 228-231, and 233-238 have been canceled without prejudice. Accordingly, Applicant respectfully requests that the rejection of claims 193-198, 212, 219-224, and 232 under 35 U.S.C. §103(a) be withdrawn.

2. Claims 200, 201, 207, 226 and 227 are rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Cheever et al. (U.S. Patent 6,664,370), Onizuka et al., Herrera et al., or Rai et al. The rejection is respectfully traversed.

Applicant submits that claims 200, 201, 207, 226 and 227 are all dependent claims depending from claims 193 and 219. As discussed above, the combination of Yan and Jamas does not render claims 193 and 219 obvious. Hence, the combination of the above cited references would also not render the above dependent claims obvious. Accordingly, Applicant respectfully requests that the rejection of claims 200, 201, 207, 226 and 227 under 35 U.S.C. §103(a) be withdrawn.

NEW REJECTION

REJECTION UNDER 35 USC § 112, 2ND PARAGRAPH

1. Claims 216-218 and 236-238 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The rejection is moot because claims 216-218 and 236-238 have been canceled without prejudice.

2. Claims 193-238 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting "pharmaceutical composition". Applicant submits that claims 193 and 219 have been amended to delete the rejected phrase. Claims 208-211, 213-218, 228-231, and 233-238 have been canceled without prejudice. Accordingly, Applicant respectfully request that the rejection of claims 193-207, 212, 219-227, 232 under 35 U.S.C. §112, second paragraph, be withdrawn.

REJECTION UNDER 35 USC § 112, 1ST PARAGRAPH

Claims 216-218 and 236-238 are rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. The rejection is moot because claims 216-218 and 236-238 have been canceled without prejudice.

REJECTION UNDER 35 USC § 103(a)

1. Claims 200, 202, 203, and 226 are rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Maloney et al.

2. Claim 205 is rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Bergman et al.

3. Claim 202 is rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Capurro et al.

4. Claims 199, 206 and 225 are rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Soiffer et al.

5. Claim 197 is rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Ren et al.

6. Claim 204 is rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Ren et al., and further in view of D'amico et al.

7. Claims 197 and 204 are rejected under 35 U.S.C. §103(a) as being unpatentable over Yan et al. (J. Immunology 163:3045-3052 (1999)) in view of Jamas et al. (U.S. patent 5,622,939), and further in view of Mendelsohn et al.

In response, Applicant submits that the above rejected claims are all dependent claims depending from claims 193 and 219. As discussed above, the combination of Yan and Jamas does not render claims 193 and 219 obvious. Hence, the combination of the above cited references would also not render the above dependent claims obvious. Accordingly, Applicant respectfully requests that the

rejection of the above dependent claims under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

Applicant respectfully maintains that all the grounds of rejections raised in the August 7, 2007 Final Office Action have been addressed and earnestly urge the Examiner to render favorable action for the claimed invention.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicant's undersigned attorney invites the Examiner to telephone him at the number provided below. No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

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